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(i) a heterologous expression control sequence which is active or can be activated in the cell and is operatively linked with a reporter gene, and

(ii) non-coding nucleic acid sequences on the 5'-side and/or the 3'-side from the region of the target gene,

(b) culturing the cell under conditions under which the expression control sequence is active, and

(c) measuring the expression of the reporter gene to determine the influence of the non-coding nucleic acid sequences on the expression of the target gene.

36. (Once Amended) A process for obtaining a DHFR-negative [eukaryotic] mammalian cell, the process comprising

(a) transfecting the cell with a first vector comprising

(i) at least one target sequence for a site-specific recombinase;

(ii) DNA sequences which flank sequence (i) and are homologous to a DHFR nucleic acid sequence which is present endogenously in the cell in order to allow a homologous recombination,

(iii) optionally a first positive selection marker gene, and

(iv) optionally a negative selection marker gene,

(b) culturing the transfected cell under conditions under which a homologous recombination of the vector takes place, and

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(c) isolating the cell obtained according to step (b) to obtain a DHFR-negative [eukaryotic] mammalian cell.

37. (Once Amended) A process for obtaining a [eukaryotic] mammalian cell containing a nucleic acid sequence to be amplified and a heterologous DHFR gene, the process comprising

(a) obtaining a DHFR-negative [eukaryotic] mammalian cell by the process as claimed in claim 36,

(b) transfecting the cell of step (a) with a second vector comprising

(i) a nucleic acid sequence coding for a DHFR,

(ii) a nucleic acid sequence to be amplified which codes for a protein in an expressible form,

(iii) optionally a second positive selection marker gene, and

(iv) at least two recombinase target sequences flanking the sequences (i), (ii) and (iii), if present,

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(c) culturing the transfected cell under conditions under which the sequences (i), (ii) and (iii), if present, are integrated into the recombinase target sequence that is already present in the genome of the cell, and

(d) isolating the cell obtained according to step (c) to obtain a [eukaryotic] mammalian cell containing a nucleic acid sequence to be amplified and a heterologous DHFR gene.

41. (Once Amended) A [eukaryotic] mammalian cell, comprising

(a) at least one inactivated endogenous nucleic acid sequence coding for a DHFR, and

(b) at least one recombinase target sequence which is integrated into the genome in the region of the sequence (a).

42. (Once Amended) The [eukaryotic] mammalian cell of claim 41, wherein the cell is a human cell.

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43. (Once Amended) A [eukaryotic] mammalian cell, comprising a heterologous nucleic acid sequence in the region of an endogenous DHFR gene locus, the heterologous sequence comprising

(i) a nucleic acid sequence coding for a DHFR,

(ii) a nucleic acid sequence coding for a desired protein, and

(iii) at least one recombinase target sequence.

REMARKS

Claims 20-43 are currently pending. In this Response, applicants amend claims 35-37 and 41-43. Claims 20-43, as amended, are presented for reconsideration.

Claim 35 is rejected under 35 USC §112, second paragraph, as being